

Listing of Claims.

Please amend the claims as shown below prior to examination.

1. (Original) A method of treating diabetes comprising administering a compound that reduces skeletal muscle ketone levels to a diabetic subject in a therapeutically effective amount to reduce skeletal muscle ketone levels.
2. Canceled.
3. (Original) The method of Claim 1, wherein the compound enhances ketolytic activity in skeletal muscle.
4. (Original) The method of Claim 3, wherein the compound enhances the activity of a ketolytic enzyme in skeletal muscle.
5. (Original) The method of Claim 1, wherein the compound reduces ketogenic activity in skeletal muscle.
6. (Original) The method of Claim 5, wherein the compound reduces the activity of a ketogenic enzyme in skeletal muscle.
7. (Original) The method of Claim 1, wherein the compound enhances hepatic fatty acid oxidation.
8. (Original) The method of Claim 7, wherein the compound enhances the activity of a hepatic fatty acid oxidizing enzyme.
9. (Original) The method of Claim 1, wherein the compound is a succinate ester or a succinate precursor.

10. (Currently amended) The method of Claim 1 ~~any of Claims 1-8~~, wherein the compound is a polypeptide.

11. (Original) The method of Claim 9, wherein the compound is an antibody.

12. (Currently amended) The method of Claim 1 ~~any of Claims 1-8~~, wherein the compound is a nucleic acid molecule.

13-14. Canceled.

15. (Original) A delivery vector comprising a heterologous nucleic acid that encodes a ketolytic enzyme, wherein the heterologous nucleic acid is operably linked to a control element that directs the expression of the nucleic acid in skeletal muscle cells.

16. (Original) The delivery vector of Claim 15, wherein the ketolytic enzyme is selected from the group consisting of acetoacetate:succinyl CoA:3oxoacid CoA transferase (SCOT) and α -ketoacid dehydrogenase.

17-18. Canceled.

19. (Original) A delivery vector comprising a heterologous nucleic acid that encodes an enzyme that mediates fatty acid oxidation, wherein the heterologous nucleic acid is operably linked to a control element that directs the expression of the nucleic acid in hepatic cells.

20. (Original) The delivery vector of Claim 19, wherein the enzyme that mediates fatty acid oxidation is selected from the group consisting of malonyl CoA decarboxylase, carnitinepalmitoyltransferase I, carnitinepalmitoyltransferase II,

carnitine acyltranslocase, acyl-CoA dehydrogenase, enoyl-CoA hydratase, 3-L-hydroxyacyl-CoA dehydrogenase, and β -ketoacyl-CoA thiolase.

21-22. Canceled.

23. (Original) An inhibitory oligonucleotide that is at least 8 nucleotides in length and specifically hybridizes to a target sequence encoding a ketogenic enzyme and reduces production of the ketogenic enzyme.

24. (Original) The inhibitory oligonucleotide of Claim 23, wherein the ketogenic enzyme is selected from the group consisting of β -hydroxybutyrate dehydrogenase, mitochondrial HMG-CoA synthase, acetoacetyl-CoA thiolase, and HMG-CoA lyase.

25-31. Canceled.

32. (Currently amended) A pharmaceutical formulation comprising the delivery vector of Claims 15 ~~any of Claims 15-18~~ in a pharmaceutically acceptable carrier.

33. (Currently amended) A pharmaceutical formulation comprising the delivery vector of Claim 19 ~~any of Claims 19-22~~ in a pharmaceutically acceptable carrier.

34. (Currently amended) A pharmaceutical formulation comprising the inhibitory oligonucleotide of Claim 23 ~~any of Claims 23-30 or the delivery vector of Claim 31~~ in a pharmaceutically acceptable carrier.

35. (Currently amended) A method of reducing ketone levels in a skeletal muscle cell comprising contacting the skeletal muscle cell with a delivery vector according to Claim 15 ~~any of Claims 15-18 or 31, an inhibitory oligonucleotide~~

~~according to any of Claims 23-30, or a pharmaceutical formulation according to Claim 32 or Claim 34 in an amount effective to reduce ketone levels in the skeletal muscle cell.~~

36-42. Canceled.

43. (Currently amended) A method of treating diabetes comprising administering a delivery vector according to Claim 15 ~~any of Claims 15-18 or 31, an inhibitory oligonucleotide according to any of Claims 23-30, pharmaceutical formulation according to Claim 32 or Claim 34~~ to a diabetic subject in a therapeutically effective amount to reduce skeletal muscle ketone levels.

44-46. Canceled.

47. (Currently amended) A method of reducing ketone levels in skeletal muscle comprising administering a delivery vector according to Claim 19 ~~any of Claims 19-22 or a pharmaceutical formulation according to Claim 33~~ to a subject in an amount effective to reduce skeletal muscle ketone levels.

48. (Currently amended) A method of treating diabetes comprising administering a delivery vector according to Claim 19 ~~any of Claims 19-22 or a pharmaceutical formulation according to Claim 33~~ to a diabetic subject in a therapeutically effective amount to reduce skeletal muscle ketone levels.

49-51. Canceled.

52. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising
contacting a ketogenic enzyme with a compound; and

detecting binding of the compound to the ketogenic enzyme, wherein binding to the ketogenic enzyme identifies the compound as a candidate for the treatment of diabetes.

53. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising
contacting a ketogenic enzyme with a compound; and
detecting a reduction in ketogenic enzyme activity, wherein a reduction in ketogenic enzyme activity identifies the compound as a candidate for the treatment of diabetes.

54. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:
contacting a cell that produces ketones with a compound;
detecting ketone levels in the cell, wherein a reduction in ketone levels identifies the compound as a candidate for the treatment of diabetes.

55. Canceled.

56. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:
contacting a cell that produces a ketogenic enzyme with a compound;
detecting an indicia selected from the group consisting of:
(a) the concentration of the ketogenic enzyme,
(b) the ketogenic enzyme activity,
(c) the level of mRNA encoding the ketogenic enzyme, and
(d) any combination of (a) to (c),
wherein a reduction in the level of the indicia in the cell identifies the compound as candidate for the treatment of diabetes.

57-58. Canceled.

59. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:
administering a compound to a mammalian subject,
detecting skeletal muscle ketone levels in the mammalian subject, wherein a reduction in skeletal muscle ketone levels identifies the compound as a candidate for the treatment of diabetes.

60. Canceled.

61. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:
administering a compound to a mammalian subject,
detecting an indicia in skeletal muscle selected from the group consisting of:
(a) the concentration of a ketogenic enzyme,
(b) a ketogenic enzyme activity,
(c) mRNA encoding a ketogenic enzyme, and
(d) any combination of (a) to (c),
wherein a reduction in the level of the indicia in skeletal muscle identifies the compound as a candidate for the treatment of diabetes.

62-63. Canceled.

64. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:
administering a compound to a transgenic non-human mammal that exhibits insulin resistance, the transgenic non-human mammal comprising an isolated nucleic acid encoding a ketogenic enzyme,
detecting the level of insulin resistance in the transgenic non-human mammal after administration of the compound, wherein a reduction in the level of insulin resistance identifies the compound as a candidate for the treatment of diabetes.

65. Canceled.

66. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising
contacting an enzyme that mediates fatty acid oxidation with a compound;
and
detecting binding of the compound to the enzyme, wherein binding to the enzyme identifies the compound as a candidate for the treatment of diabetes.

67. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising
contacting an enzyme that mediates fatty acid oxidation with a compound;
and
detecting an enhancement in enzyme activity, wherein an enhancement in enzyme activity identifies the compound as a candidate for the treatment of diabetes.

68. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:
contacting a cell that produces an enzyme that mediates fatty acid oxidation with a compound;
detecting an indicia selected from the group consisting of:
(a) the concentration of the enzyme,
(b) the enzyme activity,
(c) the level of mRNA encoding the enzyme, and
(d) any combination of (a) to (c),
wherein an enhancement in the level of the indicia in the cell identifies the compound as candidate for the treatment of diabetes.

69-70. Canceled.

71. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:

- administering a compound to a mammalian subject,
- detecting an indicia in skeletal muscle selected from the group consisting of:
 - (a) the concentration of an enzyme that mediates fatty acid oxidation,
 - (b) the activity of an enzyme that mediates fatty acid oxidation,
 - (c) mRNA encoding an enzyme that mediates fatty acid oxidation, and
 - (d) any combination of (a) to (c),

wherein an enhancement in the level of the indicia in skeletal muscle identifies the compound as a candidate for the treatment of diabetes.

72-73. Canceled.

74. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:

- administering a compound to a transgenic non-human mammal that exhibits insulin resistance, the transgenic non-human mammal comprising an isolated nucleic acid encoding an enzyme that mediates fatty acid oxidation,
- detecting the level of insulin resistance in the transgenic non-human mammal after administration of the compound, wherein a reduction in the level of insulin resistance identifies the compound as a candidate for the treatment of diabetes.

75. Canceled.

76. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising

- contacting a ketolytic enzyme with a compound; and
- detecting binding of the compound to the ketolytic enzyme, wherein binding to the ketolytic enzyme identifies the compound as a candidate for the treatment of diabetes.

77. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising
contacting a ketolytic enzyme with a compound; and
detecting an enhancement in ketolytic enzyme activity, wherein an enhancement in ketolytic enzyme activity identifies the compound as a candidate for the treatment of diabetes.

78. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:
contacting a cell that produces a ketolytic enzyme with a compound;
detecting an indicia selected from the group consisting of:
(a) the concentration of the ketolytic enzyme,
(b) the ketolytic enzyme activity,
(c) the level of mRNA encoding the ketolytic enzyme, and
(d) any combination of (a) to (c),
wherein an enhancement in the level of the indicia in the cell identifies the compound as candidate for the treatment of diabetes.

79-80. Canceled.

81. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:
administering a compound to a mammalian subject,
detecting an indicia in skeletal muscle selected from the group consisting of:
(a) the concentration of a ketolytic enzyme,
(b) the activity of a ketolytic enzyme,
(c) mRNA encoding a ketolytic enzyme, and
(d) any combination of (a) to (c),
wherein an enhancement in the level of the indicia in skeletal muscle identifies the compound as a candidate for the treatment of diabetes.

82-83. Canceled.

84. (Original) A method of identifying a candidate compound for the treatment of diabetes, comprising:

- administering a compound to a transgenic non-human mammal that exhibits insulin resistance, the transgenic non-human mammal comprising an isolated nucleic acid encoding a ketolytic enzyme,
- detecting the level of insulin resistance in the transgenic non-human mammal after administration of the compound, wherein a reduction in the level of insulin resistance identifies the compound as a candidate for the treatment of diabetes.

85. Canceled.